REMARKS

This response is responsive to the Final Office Action dated October 5, 2004, and is also being submitted as the "submission" under 37 C.F.R. § 1.114 in support of the Request for Continuing Examination being submitted together with this response.

Applicants respectfully request reconsideration of the present application in view of the foregoing remarks.

Claims 21-54 are pending.

I. Claim Rejections – 35 U.S.C. § 112, First Paragraph

Claims 21-54 stand rejected under 35 U.S.C. § 112, first paragraph, because the examiner argues that the claims are not properly enabled. Specifically, the examiner argues that "the specification, while being enabling for a transgenic mouse, does not reasonably provide enablement for any non-human animal." Office action at 2. The examiner proffers a number of reasons to support the conclusion of non-enablement, including the allegation that "applicants have ignored the fact that all [the references of record] used specific methods, specific steps and specific constructs." Office action at 3. The examiner further argues that the references of record "do not show that any one method and construct could be used for making any animal." Applicants respectfully traverse this ground of rejection.

a. The specification provides sufficient guidance to allow a skilled artisan to make the claimed "non-human transgenic animal" without undue experimentation

The specification provides extensive guidance to allow a skilled artisan to make the claimed transgenic animals without undue experimentation.

The specification provides detailed working examples illustrating how to make the claimed invention. For example, the working examples describe how to select a Tet repressor, how to make a tetracycline inducible transcriptional activator, how to make a tetracycline regulated transcriptional inhibitor fusion protein, and how to use the claimed components to regulate expression. *See, e.g.,* Bujard at 53, l. 5 – 63, l. 31. In addition, the examples describe the production of a transgenic mouse. *Id.* at 61, l. 20 – 63, l. 31.

In addition to the working examples, the specification contains extensive description of how to make the components of the inducible regulatory system and how to make transgenic animals, in addition to mice, using the claimed components. *See, e.g.*, Bujard at 6, l. 11 – 7, l. 13. For example, the specification teaches that "[a] transgenic animal can be created, for example, by introducing a nucleic acid encoding the fusion protein ... into the male pronuclei of a fertilized oocyte, e.g., by microinjection, and allowing the ooocyte to develop in a pseudopregnant female foster animal." *Id.* at 18, l. 3-6. The specification further references two patents, U.S. Patent Nos. 4,736,866 and 4,870, 009, and a well-known laboratory manual, Hogan *et al.*, A LABORATORY MANUAL (1986), to provide details of how to create a transgenic manual. The patents and laboratory manual provide a skilled artisan with step by step methodologies for implementing the DNA microinjection method of making transgenic animals.

Even if the exemplary methods described in the specification, *e.g.*, DNA injection, require some kind of experimentation from animal to animal, that experimentation would be routine in the cloning arts and not an undue burden. Specifically, the knowledge of how to perform DNA injection was well-known in the art as evinced by the references cited discussing DNA injection. A skilled artisan would only need to make routine modifications of the well-known methodologies to successfully perform the technique in different animals. Accordingly, the experimentation requires is merely routine and not undue.

b. The state of the art at the time of invention shows that transgenic animals were produced using established methods without undue experimentation

Contrary to the examiner's assertion, the references of record support the conclusion that a skilled artisan could make the claimed transgenic animals at the time of filing without undue experimentation. As noted in the Amendment filed July 16, 2004, the references of record indicate that a skilled artisan could predictably produce transgenic animals using standard techniques.

In addition, Exhibits A-G enclosed with this amendment show that a single method, *i.e.*, DNA injection, can be used to produce a broad range of transgenic animals using different constructs. Specifically, Applicants enclose abstracts of articles showing the routine

production of transgenic animals. Specifically, Applicants enclose abstracts of the following articles: Guyomard *et al.*, BIOCHIMIE 71(7):857-63 (1989) (Exhibit A); Stuart *et al.*, DEVELOPMENT 109(3):577-84 (1990) (Exhibit B); Ozato *et al.*, CELL DIFFER. 90(4):37-44 (1986) (Exhibit C); Steinbeisser *et al.*, NUCLEIC ACIDS RES. 16(8):3223-38 (1988) (Exhibit D); Knight *et al.*, PROC. NAT. ACAD. SCI. USA 85(9):3130-34 (1988) (Exhibit E); Ebert *et al.*, MOL. ENDOCRINOL. 2(3):277-83 (1099) (Exhibit F); and Pursel *et al.*, VET. IMMUNOL. IMMUNOPATHOL. 17(1-4):303-12 (1987) (Exhibit G). Each of these references describes the successful production of transgenic animals using a DNA injection technique. As noted above, the present specification also describes the use DNA injection to product transgenic animals.

The examiner argues that significant limitations, such as longer gestation times, reduced litter sizes, and low efficiency of gene integration, accompany even current transgenic technology. Office action at 4 (referencing Office action mailed January 16, 2004 at 3-5). Thus, the examiner concludes that production of transgenic animals is unpredictable and that the specification does not provide sufficient guidance to make the claimed transgenic animals without undue experimentation. Office action at 3-4.

However, the enablement requirement does not require that a skilled artisan be able to make an invention flawlessly on a commercial scale. Instead, the enablement requirement merely requires a skilled artisan be able to make and use the claimed invention without undue experimentation. MPEP § 2164. Even if complex experimentation is required, the experimentation is not necessarily undue. MPEP § 2164.01. In this case, the references of record show that transgenic animals were routinely produced at the time of filing, despite the issues identified by the examiner. Thus, the claimed transgenic animals could be produced by the skilled artisan using only routine experimentation.

c. The claims are enabled

A skilled artisan would be able to practice the claimed invention at the time of filing without undue experimentation. Specifically, the specification provides extensive guidance of how to make the claimed invention. The references of record evince that production of

transgenic animals at the time of filing required merely routine experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of this ground of rejection against claims 21-54 under 35 U.S.C. § 112, first paragraph.

II. Claim Rejections – 35 U.S.C. § 112, Second Paragraph

Claims 21, 24-27, and 29-32 stand rejected under 35 U.S.C. § 112, second paragraph, because the examiner argues that the term "detectable levels" "is a relative word and the metes and bounds of the term cannot be determined therefore it is unclear."

The term "detectable levels" is clear and definite to one of skill in the art. One of skill in the art would understand that different methods can be used to assess "detectable levels" depending on the particular application and further understand the limits of the different methods. For example, the specification discloses enzyme linked immunosorbent assays (ELISA) as one method for monitoring the expression of the regulated protein. A skilled artisan would clearly understand the limits of ELISA and be able to determine what constitutes a "detectable level[]." Accordingly, "detectable levels" is clear and definite. Thus, Applicants respectfully request this ground of rejection against claims 21, 24-27, and 29-32 under 35 U.S.C. § 112, second paragraph, be withdrawn.

III. Claim Rejections – Double Patenting

Claims 21, 24-27, and 29-54 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 5,912,411. Claims 22, 23, and 28 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 5,866,755.

Applicants will address these issues upon the claims being found allowable.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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